

Hyper-IgE Syndromes or Severe Atopic Dermatitis?

Diagnostic Procedures and Management

The appropriate diagnostic procedure to delineate severe atopic dermatitis from Hyper-IgE Syndromes is an art. The final diagnosis is best obtained on interdisciplinary grounds by dermatologists, allergologists and specialists of immunodeficiency. None specialist, however, are key to rise the first suspect and proceed with the right diagnostic procedures. This includes complete medical history asking for other atopic diseases beside eczema, a tendency towards recurrent bacterial, fungal, and viral infection, pneumonias, and for a pedigree with the question of similar symptoms in the family and consanguinity. Careful clinical examination including full body inspection is mandatory.

Findings	Atopic Dermatitis	Hyper-IgE Syndromes		
		STAT3-HIES	DOCK8-HIES	TYK2-HIES
Trade of inheritance	multi-factorial	autosomal dominant	autosomal recessive	autosomal recessive
Elevated Serum IgE	+/++	++	++	++
Blood eosinophilia	+/++	++	++	++
Eczema	++	+/++	++	+
Allergic rhinitis, food allergy etc.	++	∅	++	+
Newborn rash	-/+	+	+	+
Skin abscess(es)	∅	++	++	+
Internal abscess(es)	∅	+	+	+
Pneumonia	∅	++	++	+
Pneumatocoeles	∅	++	+	∅
Increased susceptibility to infections	+	++	++	+
Severe infections	-	+	++	+
Oral candidiasis	∅	+	+	+
Nail/mucocutaneous candidiasis	∅	+	+	+
Recurrent viral infections (VZV, HSV, Molluscum contagiosum)	++	∅	++	+
Pathologic second dentition	∅	+	∅	∅
Atypical mycobacterial infection (MOTT)	∅	-/+	∅	+
Lymphopenia	∅	∅	++	∅
Fractures w/o adequate trauma	∅	+	∅	∅
Scoliosis	∅	+	∅	∅
Hyperextensible joints	∅	+	∅	∅
Characteristic facies	∅	++	∅	∅
Increased risk of malignancy	-/+	-/+	++	?

Diagnostic procedures

- (1) Blood count including differential
- (2) Immunoglobulin levels of IgA, IgM, IgG, and total serum IgE
- (3) Test for viral, bacterial and fungal colonization or infection; don't forget nasal swab as key reservoir
- (4) If allergic symptoms or history present: perform skin prick test, hapten patch test, atopy patch test, allergen specific in vitro IgE analysis, food challenge procedures as indicated
- (5) In case of recurrent infections or suspected immunodeficiency
 - => CONTACT SPECILIZED CENTER to obtain specific diagnostic tests such as lymphocyte phenotype and function including TH17-Zell counts and B cell subsets, specific antibody production and include additional tests if necessary;
- (6) Proceed with molecular diagnostic if indicated

Treatment essentials of

Atopic Dermatitis

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|-----------------------------|---|
| Basic therapy | - restoration of epidermal barrier with emollients |
| Allergen avoidance | - following proper diagnostic procedures |
| Anti-inflammatory treatment | - reactive or proactive approach with topical corticosteroids or topical calcineurin inhibitors according to guidelines |

Hyper-IgE Syndromes

- Basic therapy for restoration of epidermal barrier
- Anti-inflammatory treatment with minimal effective regimen (avoid steroid ointment if possible)
- Early surgery of abscesses formation **except for** pneumatoceles
- Infection prophylaxis with:
 - Antibiotics (cephalosporin 2nd Generation or cotrimoxazole)
 - Antifungals if symptoms are present (e.g. fluconazole)
 - Antiviral prophylaxis recommended in DOCK8-HIES (e.g. aciclovir)
- Immunoglobulin supplementation recommended in DOCK8-HIES; to be discussed in other forms
- Consider bone marrow transplantation, which is recommended for DOCK8-HIES (limited experience yet)

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